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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/680,690	10/06/2000	David B. Weiner	UPN-3906	1044

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EXAMINER	
LI, QIAN J	
ART UNIT	**PAPER NUMBER**
1632	15

DATE MAILED: 07/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/680,690	WEINER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/21/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10-13,32-34 and 37-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10-13,32-34 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed on 4/21/03 has been entered and assigned as Paper #14. Claims 2, 32, 35, and 36 have been canceled. Claims 1, 8, 10-13, 32, and 37-42 have been amended. It is noted that claim 32 has been canceled and at the same time listed as amended in Paper #14. Further clarification is required. For the interest of compact prosecution, claim 32 has been treated as amended. Claims 1, 3-6, 8, 10-13, 32-34, and 37-42 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and new grounds of rejection will not be reiterated. The arguments of paper #14 would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

ENABLEMENT REQUIREMENT

Claims 1, 3-6, 8, 10-13, 32-34, and 37-42 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record and following.

Applicants are reminded that the claims clearly or implicitly drawn to therapeutic methods for genetic vaccination and gene therapy, thus, have been evaluated by the standard.

In paper #14, applicants argue with respect to the teaching of *Guibinga et al* that Guibinga reference refers to blocking CD28 signaling pathway in order to prevent immune responses against an adenoviral vector used for gene transfer while applicants are not suggesting effecting CD28 signaling pathway at all.

The argument has been fully considered but found not persuasive. This is because when the CD28 is used as a ligand engaging the CD80/CD86 on the surface of the immune cell, the CD28 signaling pathway would be triggered regardless the intention of applicants, and the claims encompass using an adenoviral vector for gene transfer, thus, claimed invention clearly contradict the cited teaching. Moreover, the amended claims are limited to using CD28 as targeting ligand for introducing a nucleic acid into a CD80 and/or CD86 expressing cells, which are immune cells such as lymphocytes, monocytes, and dendritic cells. The claims encompass delivering *non*-immunogenic protein to these cells for gene therapy, however, upon engaging the CD28 with CD80/86, a non-specific immune response would triggered, and the delivered protein would be eliminated as seen in the teaching of *Guibinga et al*. Thus, it is highly unpredictable and the specification fails to teach whether the therapeutic gene could be sufficiently delivered and whether a therapeutic effect could be achieved, thus, fails to provide an enabling disclosure to support the full scope of the claims.

In paper #14, applicants also argue, with respect to the teaching of Deonarian, that reference to Deonarian indicates that the technology does work but at a less than optimal level. The argument has been fully considered but found not persuasive. This is because the claims are clearly and implicitly drawn to a therapeutic method delivering therapeutic proteins to a subject, and a less than optimal level of gene delivery is unlikely to result in a therapeutic effect to enable the instant invention, particularly considering other con factors known to prevent effective gene delivery such as the teachings of *Guibinga et al*, *McCluskie et al, Torres et al, and Nakano et al.*

In paper #14, applicants further argue, with respect to the teaching of *McCluskie et al, Torres et al, and Nakano et al,* that none provide any support to question Applicants assertion that the claimed invention is enabled. The argument has been fully considered but found not persuasive. This is because the specification is silent with regard to the general aspect of routes of gene delivery, prophetically teaches targeted delivery, and only illustrated co-expressing of cytokine molecules with an immunogenic protein in a plasmid (1st paragraph, page 40, examples) by intramuscular rejection, and *Nakano et al* teach that immune reactivity with plasmid DNA encoding antigenic domains is linked to the injection mode, "DIFFERENT ROUTES OF INJECTION OF HCV E2 PLASMID CAN RESULT IN QUANTITATIVELY AND QUALITATIVELY DIFFERENT HUMORAL IMMUNE RESPONSES" Applicants are reminded that 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In re Fisher, 166 USPQ 18, 24 (CCPA 1970). In the instant case, the art of record (*Guibinga et al, Capon et al and Hurwitz et*

al) teaches away from the full scope of the instant claims, thus, it is incumbent upon applicants to provide sufficient guidance within the specification to support the full scope of the invention. "WHEN CONSIDERING THE FACTORS RELATING TO A DETERMINATION OF NON-ENABLEMENT, IF ALL THE OTHER FACTORS POINT TOWARD ENABLEMENT, THEN THE ABSENCE OF WORKING EXAMPLES WILL NOT BY ITSELF RENDER THE INVENTION NON-ENABLED." "LACK OF A WORKING EXAMPLE, HOWEVER, IS A FACTOR TO BE CONSIDERED, ESPECIALLY IN A CASE INVOLVING AN UNPREDICTABLE AND UNDEVELOPED ART." (MPEP 2164.02, 03)

Therefore, for reasons of record and those set forth above, the instant specification fails to meet the statutory enablement requirement set forth under 35 U.S.C. §112, 1st paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10, 33, 34, 37-42 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are vague and indefinite because claim 33 recites the limitation "the viral protein portion". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 10, 11, and 13 are newly rejected under 35 U.S.C. 102(e) as being anticipated by *Wong-Staal et al* (US 2001/0007659).

Wong-Staal et al teach a method of introducing a nucleic acid molecule, a lentiviral vector, into a dendritic cell that expresses CD80 and/or CD86 (page 4, paragraph 0031) comprising incorporating a binding domain for CD86 including CD28 (containing the extracellular region) in the coat protein of the retrovirus (a viral particle) comprising the lentiviral vector, and administering such to a cell (examples 4 & 6) or a subject (example 7). Therefore, *Wong-Staal et al* anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8, 12, 32-34, 41, and 42 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Wong-Staal et al* (US 2001/0007659), in view of *Paul et al* (US 5,736,387).

Wong-Staal et al teach a method of introducing a nucleic acid molecule into a dendritic cell that expresses CD80 and/or CD86 using CD28 as a targeting ligand. *Wong-Staal et al* do not teach a fusion ligand.

Paul et al teach a chimeric (fusion) targeting ligand for directing gene delivery to a specific mammalian cells, wherein the ligand comprising a ligand moiety capable of binding to receptors present on target cells, and an uptake moiety capable of promoting entry of the vector into the target cell (abstract), wherein the ligand moiety could be any cytokine and analog (column 10, line 34-39), wherein the uptake moiety could be the gp41 of HIV virus including the cytoplasmic and transmembrane regions (column 16, particularly line 52). *Paul et al* do not specifically teach the CD28 ligand.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods taught by *Wong-Stall et al and Paul et al*, by simply selecting CD28 as the ligand moiety for dendritic cell targeting with a reasonable expectation of success. The ordinary skilled artisan would have been

motivated to modify the claimed invention because the gp41 uptake moiety in the chimeric targeting protein provides additional means for delivering nucleic acids into the cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 3-6, and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Wong-Staal et al* (US 2001/0007659) and *Paul et al* (US 5,736,387) as applied to claims 1, 8, 12, 32-34, 41, and 42 above, and further in view of *Sedlacek et al* (US 6,358,524).

The combined teachings of *Wong-Staal et al* and *Paul et al* do not teach delivering a DNA molecule.

Sedlacek et al teach a method for inserting genes into cells comprising delivering a complex into cells of an organism (abstract). The complex comprising a non-viral carrier such as cationic amphiphile/DNA complex (column 5, lines 26-67 and column 21, lines 54-64); a ligand that binds specifically to the desired target cell such as membrane receptors on the surface of immune cells (column 9, lines 9-16); a fusion protein for the penetration of the vector into the cytoplasm of the target cell, such as fusogeneic protein gp41 (column 17, lines 14-19); and the gene to be introduced in the form of nucleic acid containing the corresponding gene (immunogenic or non-immunogenic) provided with regulatory regions, preferably as a plasmid (column 5, lines 20-25). *Sedlacek et al* do not specifically teach the CD28 receptor ligand or fusing the components of the complex.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods taught by *Wong-Stall et al, Paul et al, and Sedlacek et al*, by simply selecting CD28 as the ligand moiety for delivering a DNA molecule to dendritic cells and fusing the ligand with the fusogenic gp41 with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the gp41 uptake moiety in the chimeric targeting protein provides additional means for gene delivery vector entering into the cells, and it is a matter of optimization and customization for the target cells of interest. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

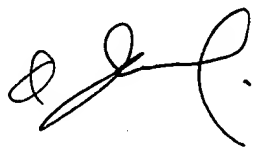
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

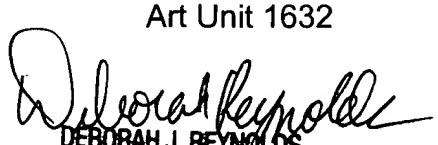
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).



Q. Janice Li
Examiner
Art Unit 1632



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QJL
July 11, 2003